REMARKS

Upon entry of this amendment, claims 32, 35-39, 42, 45-49, 52-55, 84 and 89-90 are pending. Claims 1-31, 56-83 and 86-88 were cancelled, without prejudice or disclaimer, as being drawn to non-elected inventions. Claims 33-34, 40-41, 43-44, 50-51 and 85 were cancelled, claims 32, 42, 52-53, and 84 were amended and new claims 89-90 were added. Support for the amendment to claim 42 can be found in claims 1, 2 and 6 as-filed and in the specification at, *e.g.*, page 2, line 28 to page 3, line 7; and page 4, lines 14-20. Support for the amendment to claim 52 can be found in the specification at, *e.g.*, page 9, lines 28-31. Support for the amendment to claim 53 can be found in the specification at, *e.g.*, page 9, lines 28-31. Support for the amendment to claim 84 can be found in the specification at, *e.g.*, page 17, lines 1-3. Support for new claims 89-90 can be found in claims 54-55 as-filed. Thus, no new matter has been added.

Inventorship

Applicants believe that a correction of inventorship may be necessary and will file a Petition to Correct Inventorship shortly.

Election/Restrictions

Applicants note that claims 32, 35-39, 42, 45-49, 52-55, 84 and 89-90 are currently under examination in this case. Claims 1-31, 56-83 and 86-88 have been cancelled herein without prejudice or disclaimer, as being drawn to a nonelected invention.

Priority

Applicants thank the Examiner for noting that this application claims the benefit of priority to U.S. Provisional application 60/043,609, filed on April 15, 1997.

Claim Rejections -- 35 U.S.C. § 112

Second paragraph.

Claims 32-55, 84 and 85 have been rejected under 35 U.S.C. § 112, second paragraph as being indefinite. According to the Examiner, the claims are vague and indefinite because of the claim limitation "at the expense."

Applicants have amended claims 32 and 42 herein to remove the limitation "at the expense." Rather, these claims now specify that the antigen-specific immune effector cells are expanded in culture by culturing these immune effector cells with hybrid cells. Thus, these claims, as amended herein, are not indefinite and this rejection of these claims should be withdrawn.

Claims 34 and 44 have been rejected under 35 U.S.C. § 112, second paragraph as being indefinite. According to the Examiner, the claims are vague and indefinite because it is unclear which type of cell the claim recitation "the cells" refers to.

Applicants have cancelled claims 34 and 44. The limitation of claim 34 has been incorporated into claim 32, as amended herein, and the limitation of claim 44 has been incorporated into claim 42, as amended herein. Thus, this rejection of these claims is moot and should be withdrawn.

Claim 52 has been rejected under 35 U.S.C. § 112, second paragraph as being indefinite. According to the Examiner, the claim is vague and indefinite because of the claim limitation "naive."

Applicants have herewith amended claim 52 to recite '[t]he population according to claim 42, wherein the immune effector cells are naïve prior to culturing said immune effector cells with hybrid cells." Support for this amendment is found in the specification at, *e.g.*, page 9, lines 28-31. Moreover, claim 53 has been amended herein to recite "[t]he population according to claim 42, wherein the immune effector cells are educated prior to culturing said immune effector cells with hybrid cells." Support for this amendment is found in the specification at, *e.g.*, page 9, lines 28-31. Thus, Applicants contend that these claims, as amended, are not vague or indefinite. Therefore, the rejection of claim 52 on this ground has been overcome and should be withdrawn.

First paragraph.

Claims 32-55, 84 and 85 have been rejected under 35 U.S.C. § 112, first paragraph for lack of enablement. According to the Examiner, "the specification, while being enabling for using the educated immune effector cells as a vaccine in a mouse tumor model, does not reasonably provide enablement for using such a vaccine in humans." (See Office Action, page 3).

Applicants have cancelled claims 33-34, 40-41, 43-44, 50-51 and 85. Thus, this rejection as it applies to these claims is moot and should be withdrawn.

Moreover, Applicants have amended claims 84 herein to remove the limitation "vaccine" and to instead recite "composition." Contrary to the Examiner's contention, Applicants assert that the composition of claim 84, as amended herein, as well as the populations of educated, antigen-specific immune effector cells of claims 32, 35-39, 42, 45-49, 52-55 and 89-90 are not limited to therapeutic uses in humans. For example, the specification discloses that the antigen-specific immune effector cells are useful in antigen discovery techniques, including methods for identifying a polynucleotide fragment of a gene that encodes an antigen recognized by the population of antigen-specific immune effector cells. (*See, e.g.*, page 26, line 24 to page 32, line 33). Also, antigen-specific immune effector cells are useful in methods of screening candidate peptides for antigenic activity. (*See, e.g.*, page 33, line 1 to page 36, line 28.)

Thus, Applicants contend that the claimed invention is not limited to therapeutic uses. Moreover, the specification fully enables the instant claims, as those skilled in the art would be able to make and use the claimed educated cells and compositions without undue experimentation. MPEP § 2164.01(c), entitled "How to Use the Claimed Invention," describes how an Examiner must address issues of enablement:

> In contrast, when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use. If multiple uses for claimed compounds or compositions are disclosed in the application, than an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In other words, if any use is enabled when multiple uses are disclosed, the application is enabled for the claimed invention.

Here, the specification enables several uses for the claimed invention. Thus, because claims 32, 35-39, 42, 45-49, 52-55, 84 and 89-90 are fully enabled by the specification, Applicants respectfully request that this rejection be withdrawn.

Claim Rejections -- 35 U.S.C. § 102

Claims 32, 35, 42, 45 and 84 have been rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,306,388 ("Nair"). The Examiner states that "Nair et al. teach a population of CTL educated by tumor-specific antigen presenting cells, and the CTL could be administered to a patient in a method of adoptive immunotherapy." (See Office Action, page 8). Applicants traverse.

Applicants have cancelled claim 85. Thus, this rejection as it applies to claim 85 is moot. Applicants have also amended independent claims 32 and 42 to further define the hybrid cells that are cultured with the antigen-specific immune effector cells. Specifically, the hybrid cells are generated by fusion between at least one mammalian dendritic cell and at least one mammalian tumor or cancer cell that expresses a cell-surface antigen, wherein the dendritic cell and the cancer or tumor cell are from the same mammalian species, wherein the dendritic cell can process and present antigens, and wherein at least half of the hybrid cells express, in an amount effective to stimulate an immune system, (a) a MHC class II molecule, (b) B7, and (c) the cell-surface antigen.

In contrast Nair teaches that the cytotoxic T lymphocyte (CTL) can be contacted with an antigen-producing cell that is a dendritic cell, a macrophage or an endothelial cell (col. 1, lines 63-66), which has been loaded with tumor-derived or pathogen-derived RNA (col. 2, lines 55-60). Nair does not teach or suggest contacting a CTL with a hybrid cell. Moreover, Nair does not teach or suggest the use of the specific hybrid cells of the present invention, as required by claims 32 and 42 as amended herein. Therefore, Nair does not anticipate independent claims 32 or 42 since it does not teach all of the limitations of these claims.

Moreover, claims 35, 45 and 84 depend from claim 32 and/or claim 42. As such, they necessarily contain all of the limitations of the claims from which they depend. Thus, for the reasons articulated above, claims 35, 45 and 85 are also not anticipated by Nair.

Claims 32, 35, 42, 45, 84 and 85 have been rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,156,307 ("Granucci"). The Examiner states that "Granucci et al. teach production of a population of activated T-lymphocytes by co-culturing of naïve or antigen-specific T-lymphocytes with the antigen-loaded dendritic cell line, and then use the activated T cells for generating desired immune response in vivo, wherein the antigens include tumor, or pathogens... wherein the antigen-loading encompasses transferring genes coding for antigenic determinants to DCs...wherein the DCs could be further modified by other genes such as cytokine genes for modulating the immune response." (See Office Action, page 9). Applicants traverse.

Granucci teaches that T lymphocytes can be activated *ex vivo* by co-culture with an antigen-loaded dendritic cell line (col. 4, lines 59-63), the cell line being loaded by introduction of exogenous genetic material (col. 2, lines 36-41). However, Granucci does not teach or suggest contacting T lymphocytes with hybrid cells, as required by the instant claims. Further, Granucci does not teach or suggest the use of the specific hybrid cells of the present invention as is required by claims 32 and 42, as amended herein. Therefore, Granucci fails to teach all of the limitations of claims 32 and 42 and, thus, does not anticipate these claims.

Likewise, claims 35, 45 and 84 depend from claim 32 and/or 42. Thus, they necessarily contain all of the limitations of the claims from which they depend. As such, for the reasons articulated above, claims 35, 45 and 84 are also not aniticipated by Granucci. Therefore, this rejection should be withdrawn.

Claim Rejections -- 35 U.S.C. § 103

Claims 32-55, 84 and 85 have been rejected under 35 U.S.C. § 103(a) as being obvious over Granucci in view of WO96/30030 ("Moser"). The Examiner stated that "Moser et al teach hybrid cells between dendritic cells from autologous or allogeneic HLA-matched dendritic cells fused with autologous tumor cells." (See Office Action, page 9). The Examiner further states that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the fused cells of Moser et al in the process of Granucci and Moser et al with a reasonable expectation of success." (See Office Action, page 10). Applicants traverse.

Applicants have cancelled claim 85. Thus, this rejection as it applies to claim 85 is moot As discussed above, Granucci does not teach or suggest the use of the specific hybrid cells of the

present invention. The addition of Moser et al. does not cure the deficiencies of Granucci. Rather, Moser discloses tumor-dendritic cell hybrids lacking expression of B7. Moser was unable to obtain either murine (*See* page 24, lines 1-2, and Table 1) or human (*See* page 32, lines 14-15, and Table 2) fused cells that expressed B7 even though Moser used B7 expressing dendritic cells as a starting material (*See* Tables 1 and 2). Thus, Granucci in view of Moser fails to teach or suggest all of the limitations of the claimed invention. Therefore, as these references do not render these claims obvious, this rejection of these claims should be withdrawn.

CONCLUSION

Based on the instant amendments and remarks, Applicants submit that this application is in condition for allowance and such action is respectfully requested. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact Applicants' undersigned attorney at the telephone number indicated below.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

32. (Amended) A substantially pure population of educated, antigen-specific immune effector cells expanded in culture by contacting said immune effector cells with [at the expense of] hybrid cells, wherein said hybrid cells are generated by fusion between at least one mammalian dendritic cell and at least one mammalian tumor or cancer cell that expresses a cell-surface antigen, wherein the dendritic cell and the cancer or tumor cell are from the same mammalian species, wherein the dendritic cell can process and present antigens, and wherein at least half of the hybrid cells express, in an amount effective to stimulate an immune system, (a) a MHC class II molecule, (b) B7, and (c) the cell-surface antigen [wherein the hybrid cells comprise antigen presenting cells fused to cells that express one or more antigens].

33-34. (Cancelled).

40-41. (Cancelled).

42. (Amended) A substantially pure population of educated, antigen-specific immune effector cells produced by culturing immune effector cells with hybrid cells, wherein said hybrid cells are generated by fusion between at least one mammalian dendritic cell and at least one mammalian tumor or cancer cell that expresses a cell-surface antigen, wherein the dendritic cell and the cancer or tumor cell are from the same mammalian species, wherein the dendritic cell can process and present antigens, and wherein at least half of the hybrid cells express, in an amount effective to stimulate an immune system, (a) a MHC class II molecule, (b) B7, and (c) the cell-surface antigen [wherein the hybrid cells are antigen presenting cells fused to cells that express one or more antigens and wherein the educated, antigen-specific immune effector cells are expanded at the expense of the hybrid cells].

43-44. (Cancelled).

50-51. (Cancelled).

52. (Amended) The population according to claim 42, wherein the immune effector cells are naïve prior to culturing said immune effector cells with hybrid cells.

53. The population according to claim 42, wherein the immune effector cells are educated prior to culturing said immune effector cells with hybrid cells.

84. (Amended) A composition [vaccine] comprising the population of antigen-specific immune effector cells of claim 32 or 42 and a pharmaceutically acceptable carrier.

85. (Cancelled).

89. (New) The population according to claim 32, wherein the immune effector cells are produced by contacting immune effector cells with hybrid cells in the presence of a cytokine.

90. (New) The population of claim 89, wherein the cytokine is IL-2.